

# The shuttle walk exercise test in idiopathic pulmonary fibrosis

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**Abstract** The shuttle walk test (SWT) is a validated, incremental walking test for chronic obstructive pulmonary disease, but not for idiopathic pulmonary fibrosis (IPF). The measurement of maximal oxygen consumption ( $\text{VO}_2$  max) is considered to be the gold standard measurement of functional capacity. This study examines the relationship between IPF patients' performance on the SWT and  $\text{VO}_2$  max. Twenty patients were recruited for the study, which consisted of two separate experiments. Firstly, the relationship between SWT performance on a conventional corridor SWT, with that on a programmable treadmill SWT designed to reproduce the corridor SWT was examined ( $n=10$ ). In the second experiment, the relationship between performance on the treadmill equivalent SWT and  $\text{VO}_2$  max measurements was studied ( $n=10$ ). There was a significant correlation between distance walked on the corridor SWT, and that walked on the treadmill equivalent SWT without  $\text{VO}_2$  max measurements (367 m vs. 410 m) ( $r=0.91$ ,  $P=0.0003$ ). There was a significant correlation between distance walked on the treadmill equivalent SWT (277 m), and the directly determined  $\text{VO}_2$  max (14.87 ml/kg/min) ( $r=0.74$ ,  $P=0.01$ ). During both experiments, a significant correlation was also observed between baseline  $\text{PaO}_2$  and SWT performance, and between  $\text{DL}_{\text{CO}}$  and SWT performance. The shuttle walk test is a simple objective measure of functional capacity in IPF patients, which should facilitate the evaluation of new therapeutic compounds for IPF. © 2003 Elsevier Science Ltd. All rights reserved.

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## INTRODUCTION

Unlike many simple exercise tests (1,2), the shuttle walking test (SWT) is a standardized, incremental walking test, stressing the individual to a symptom limited maximal performance (3). The fact that this test is externally paced overcomes the limitations that have made other self-paced walking tests (1,2) lose favour as objective measures of functional capacity. The SWT can be carried out in any clinical unit without the need for special facilities and takes relatively little time to complete. The SWT has previously been demonstrated to be a reproducible measure of functional capacity in patients with chronic obstructive pulmonary disease (COPD) (4,5), cystic fibrosis (6), heart failure (7), and in patients with pacemakers (8); but such data is not available in patients with idiopathic pulmonary fibrosis (IPF). With the advent

of multi-centre therapeutic studies of novel compounds for IPF, a standardized tool for estimating functional capacity is vital. The measurement of maximal oxygen consumption ( $\text{VO}_2$  max) by analysis of expired air during a maximal exercise laboratory test, is considered to be the gold standard measurement of functional capacity (4), however measuring  $\text{VO}_2$  max is resource demanding. Therefore, this study was undertaken in order to provide a standardized endpoint which can be easily applied in therapeutic trials.

This study examines the relationship between IPF patients' performance on the SWT and  $\text{VO}_2$  max, employing two different approaches. In the first experiment we measured the distance walked during a conventional corridor SWT, and examined whether it was equivalent to the distance walked during a programmable treadmill test, designed to reproduce the corridor SWT. In the second experiment we made measurements of the  $\text{VO}_2$  max during the treadmill equivalent SWT. These two experiments allowed us to examine the relationship between  $\text{VO}_2$  max and performance during the SWT in IPF patients.

## METHODS

### Patient selection criteria

Out-patients with usual interstitial pneumonia (UIP)-pattern IPF were studied. All subjects gave informed consent, and the local hospital ethics committee approved the study. The diagnosis of UIP was based on either high-resolution computed tomography (HRCT) or an open lung biopsy (OLB). All patients had been treated with corticosteroids and various chemotherapeutic regimes before and after referral. Exclusion criteria were: (a) the presence of known histories of collagen vascular disease, allergic alveolitis, or exposure to organic dusts; (b) patients with a tissue diagnosis of non-specific interstitial pneumonia (NSIP)/fibrosis, desquamative interstitial pneumonia (DIP), respiratory bronchiolitis associated with interstitial lung disease (RBILD), or bronchiolitis obliterans organizing pneumonia (BOOP); (c) patients with a predominantly ground-glass attenuation on HRCT scan (9,10); and (d) patients who demonstrated an objective response to corticosteroids alone.

### HRCT scanning

All patients underwent HRCT of the chest. All HRCT scans were obtained immediately after referral, using a Picker PQ scanner (Picker International, Cleveland, OH). The HRCT scans consisted of 1.5-mm-thick slices acquired at 10-mm increments through the thorax, reconstructed with a high spatial frequency algorithm. Scans were performed at end-inspiration with the patients in the supine position; no intravenous contrast was given. HRCT criteria for diagnosing UIP were as follows (9,11): (a) a reticular pattern of intralobular interstitial thickening demonstrating a peripheral, subpleural, and basal predominance with irregular pleuroparenchymal interfaces; (b) may show areas of honeycombing and traction bronchiectasis; (c) ground-glass opacification may be present but the reticular pattern predominates; (d) consolidation and nodules must be absent.

### Surgical lung biopsies

Surgical lung biopsies were completed either through a thoracotomy incision or by video-assisted thorascopic surgery. The site of the biopsy was directed by HRCT. The diagnosis of UIP was based on the following histopathologic criteria (12): (a) a variegate picture of interstitial fibrosis, inflammation, and normal tissue; (b) tendency for fibrosis to subpleural and peripheral distribution; (c) the absence of the uniform fibrotic changes characteristic of NSIP and of features indicating other causes (e.g. asbestos bodies, granulomata).

### Lung physiology

Spirometry ( $V_{\max}$  22; Sensormedics Yorba Linda, CA), and  $DL_{CO}$  (P.K. Morgan, Rainham, England) were measured. All lung function measurements were performed in the same laboratory.  $DL_{CO}$  values were corrected to haemoglobin. Alveolar volume ( $V_A$ ) was measured by a single-breath helium dilution method, and diffusing capacity per unit volume ( $K_{CO}$ ) was calculated by dividing  $DL_{CO}$  by  $V_A$ . Values were expressed as absolute values and, where appropriate, as percentages of the predicted values calculated according to sex, weight, and age. The definitions and methods for performing lung volumes and diffusing capacity followed the recommendation of the European Coal and Steel Community.(13,14) All lung function measurements used in this study were obtained immediately before SWT.

### Study design

A prospective, randomized study of 20 out-patients with IPF was performed, which consisted of two separate experiments. In the first, we examined the relationship between shuttle test performance on a conventional corridor SWT and a programmable treadmill SWT, designed to reproduce the corridor SWT ( $n=10$ ). In the second experiment, using a different cohort of IPF patients, we examined the  $VO_2$  max during the treadmill equivalent SWT ( $n=10$ ). Table I shows the demographics of the two groups. Subjects had no impacting interventions, prior to, or during the study. For each experiment, patients were required to make two visits at the same time of day to the pulmonary laboratory at intervals of approximately 1 week. The first visit of each experiment was for the purpose of familiarization, and the patients performed one practice corridor SWT and one practice treadmill equivalent SWT according to the established protocol (3). The two experiments were performed in two different patient groups to control for the training of equipment familiarization.

### Corridor shuttle walk test

Briefly, as previously described,(3) the corridor SWT requires patients to walk at increasing speeds up and down a 10 m course using marker cones that are placed 0.5 m in from each end, avoiding the need for any abrupt change in direction. The speed of walking, increasing every minute, is controlled by audio signals played from a tape cassette. The end of the test is determined by either (a) the patient, when he or she is too breathless to maintain the required speed or (b) the operator, if the patient fails to complete a shuttle in the time allowed (that is, is more than 0.5 m away from the cone when the bleep sounds) or (c) attainment of 85% of the predicted maximal heart rate.

**TABLE 1.** Characteristics of the patients according to patient group

Evaluated parameter	Experiment 1	Experiment 2
No. of subjects	10	10
Age, year	59.1 ± 12.1	58.5 ± 12.7
Male/ female	6/4	5/5
Steroids (mg)	17.5 ± 3.5	12.2 ± 1.2
Pack years	23.7 ± 19.8	27 ± 17.9
FEV <sub>1</sub> , l	1.9 ± 0.7	1.6 ± 0.5
FEV <sub>1</sub> , %pred	71 ± 23	58 ± 13
FVC, l	2.4 ± 0.9	2.0 ± 0.7
FVC, %pred	74 ± 23	55 ± 12
DL <sub>CO</sub> , ml/min/mmHg	3.1 ± 0.4	3.8 ± 1.4
DL <sub>CO</sub> , %pred	41 ± 12	47 ± 14
K <sub>CO</sub> , mmol/kPa/min	0.9 ± 0.4	1.2 ± 1.4
K <sub>CO</sub> , %pred	69 ± 28	95 ± 21
Baseline pH	7.4 ± 0.01	7.4 ± 0.01
Baseline PaO <sub>2</sub> , kPa	8.7 ± 1.6	9.1 ± 2.2
O <sub>2</sub> desaturation, %	9 ± 4.6	7 ± 6.2
Maximum heart rate, bpm	124 ± 25	130 ± 24

\*Values are means ± SD.

### Treadmill equivalent shuttle walk test

During the treadmill equivalent SWT, a programmable powerjog machine was employed (Cardiokinetics Ltd, Salford, UK). This used a speed of 30 m/min for the first minute, with the speed increasing by 10 m/min for each subsequent minute, designed to reproduce the corridor SWT. There was no incline on the treadmill throughout the test. During both the corridor and treadmill equivalent SWT, heart rate and oxygen saturations were recorded using a portable pulse oximeter, and VO<sub>2</sub> max was recorded during the treadmill equivalent SWT by analysis of expired air using a mass-flow sensor to detect airflow with a VMAX 229 system (Sensormedics, Yorba Linda, CA). A noseclip was used throughout the entire treadmill equivalent SWT period.

During the first experiment, the two exercise tests were organized in a randomized, single blinded design, i.e. the corridor SWT or the treadmill equivalent SWT *without* VO<sub>2</sub> max measurements, both performed on the same day, with a rest period of 45 min between the tests. During the second experiment, subjects performed only the treadmill equivalent SWT test, *with* VO<sub>2</sub> max measurements.

### Statistical analysis

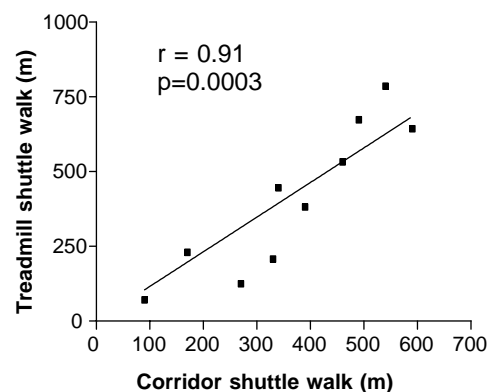
Data were shown to be normally distributed as analysed using a validated statistical software package for personal computers (Graph Pad Prism Inc., San Diego). To assess the strength of the relationship between two variables, the co-efficient of correlation (Pearson's) de-

noted by "*r*" was calculated. Values are presented as mean (CI) unless otherwise stated, and a 5% level of significance was adopted throughout.

## RESULTS

### Relationship between performance on the corridor SWT and treadmill equivalent SWT without VO<sub>2</sub> max measurement

There was a significant correlation between the distance walked on the corridor SWT, mean (CI) 367 m (252.4–481.6), and the treadmill equivalent SWT 409.9 m (232.7–587.1), (*r*=0.91, *P*=0.0003) (Fig. 1). A significant correlation was also observed between baseline PaO<sub>2</sub>, 8.7 kPa (7.4–9.9) and corridor SWT distance (*r*=0.78, *P*=0.01), and between baseline PaO<sub>2</sub> and treadmill equivalent SWT distance (*r*=0.73, *P*=0.02). There was no difference between the O<sub>2</sub> desaturation from baseline after the corridor SWT, 9% (1–18), and the treadmill equivalent SWT 9% (3–15), (*P*=0.85). There was a significant correlation between DL<sub>CO</sub>, 3.1 ml/min/mmHg (2.1–4.2) and corridor SWT distance (*r*=0.89, *P*=0.003), and between DL<sub>CO</sub> and treadmill equivalent SWT distance (*r*=0.89, *P*=0.003); however there was no relationship between K<sub>CO</sub>, 0.9 mmol/kPa/min (0.6–1.3) and corridor SWT distance (*r*=0.66, *P*=0.07), and between K<sub>CO</sub> and treadmill equivalent SWT distance (*r*=0.59, *P*=0.12). Furthermore, there was no relationship between FEV<sub>1</sub>, 1.9 l/min (1.3–2.4) and corridor SWT distance (*r*=0.34, *P*=0.41), and between FEV<sub>1</sub> and treadmill equivalent SWT distance (*r*=0.43, *P*=0.29). There was no relationship between FVC, 2.4 l/min (1.6–3.2) and corridor SWT distance (*r*=–0.004, *P*=0.99), and between FVC and treadmill equivalent SWT distance (*r*=0.009, *P*=0.98). There was no relationship between the maximum heart rate recorded after the corridor SWT, 118 bpm (94–143) and corridor SWT distance (*r*=0.35, *P*=0.49), and no relationship between the maximum heart rate recorded after



**Fig. 1.** Correlation between the performance distance on the corridor shuttle walk test and the performance distance on the treadmill equivalent shuttle walk test (*n*=10).

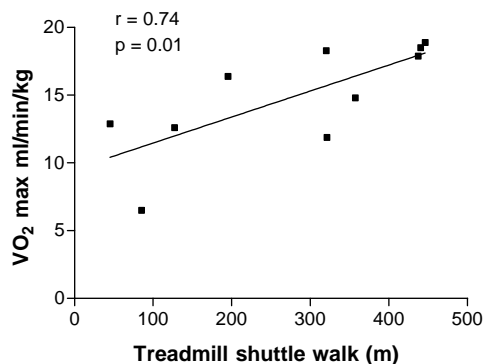
the treadmill equivalent SWT, 124 bpm (106–142) and treadmill equivalent SWT distance ( $r=0.44$ ,  $P=0.20$ ).

### Relationship between treadmill equivalent SWT and $\text{VO}_2$ max

The relationship between the distance walked on the treadmill equivalent SWT, 277.3 m (167.8–386.8), and the directly determined  $\text{VO}_2$  max 14.87 ml/kg/min (12.04–17.70) was strong ( $r=0.74$ ,  $P=0.01$ ) (Fig. 2). A significant correlation was also observed between baseline  $\text{PaO}_2$ , 9.1 kPa (7.6–10.7) and treadmill equivalent SWT distance ( $r=0.67$ ,  $P=0.03$ ). The  $\text{O}_2$  desaturation from baseline, after the treadmill equivalent SWT was 7% (1–12). There was a significant correlation between  $\text{DL}_{\text{CO}}$ , 3.8 ml/min/mmHg (2.7–4.8) and treadmill equivalent SWT distance ( $r=0.68$ ,  $P=0.03$ ), however there was no relationship between  $\text{K}_{\text{CO}}$ , 1.2 mmol/kPa/min (1.0–1.4) and treadmill equivalent SWT distance ( $r=0.15$ ,  $P=0.68$ ). Furthermore, there was no relationship between  $\text{FEV}_1$ , 1.6 l/min (1.3–2.0) and treadmill equivalent SWT distance ( $r=0.44$ ,  $P=0.20$ ). There was no relationship between FVC, 2.0 l/min (1.4–2.5) and treadmill equivalent SWT distance ( $r=0.54$ ,  $P=0.10$ ). There was no relationship between the maximum heart rate recorded after the treadmill equivalent SWT, 130 bpm (113–147) and treadmill equivalent SWT distance ( $r=0.41$ ,  $P=0.24$ ).

## DISCUSSION

The main finding from this study is that the SWT is a reliable measure of functional capacity in patients with IPF. Our data in IPF patients demonstrate a strong relationship between the distance walked during a conventional corridor SWT, and that walked during a treadmill equivalent SWT, designed to reproduce the corridor SWT. We further demonstrate, for the first time in IPF patients, a significant correlation between treadmill equivalent



**Fig. 2.** Correlation between the performance distance on the treadmill equivalent shuttle walk test and the  $\text{VO}_2$  max ( $n=10$ ).

SWT performance and  $\text{VO}_2$  max. This should facilitate the evaluation of novel therapeutic compounds.

The corridor SWT has previously been demonstrated to be a reproducible measure of functional capacity in patients with chronic obstructive pulmonary disease (3). A patient's maximal oxygen consumption plays a decisive role in his or her physical performance (15) and is regarded as the best physiological measurement of endurance performance. However, the pathophysiology of COPD and IPF are different. In IPF, the fall in  $\text{PaO}_2$  with exercise is due to a combination of ventilation–perfusion mismatch, shunt, and alveolar–capillary diffusion limitation (16–18); whereas in COPD, the major contributing factor to hypoxemia with exercise is inadequate ventilatory response causing the  $\text{PaCO}_2$  to rise and the  $\text{PaO}_2$  to fall (16). Therefore, although the SWT is accepted as a validated tool for estimating exercise capacity in COPD, (3) it could not, until now, be assumed to be a valid measure in IPF patients.

All the patients in our study reported that breathlessness was the major factor in stopping the test. Cardiovascular factors appeared to be relatively unimportant in limiting the exercise tolerance, as the maximal heart rates were lower than predicted values anticipated for the patients' age, suggesting a ventilatory limit to exercise. It has recently been demonstrated that the SWT is a reproducible method for evaluating the impact of shortness of breath on functional capacity in ambulant patients with advanced cancer (19). Furthermore, the reversal of deconditioning as a contribution to improving breathlessness in COPD is an important part of pulmonary rehabilitation. (20) The evidence for the general benefits of exercise is becoming clear from many branches of medicine (21,22) and should not be neglected in IPF patients.

The assessment of exercise capacity in patients with IPF potentially provides an objective index of their disability and reveals functional abnormalities not obvious in lung function measurements made at rest. It would seem reasonable to suggest that patients' static lung function test results should relate well to their exercise ability, but this is not the case. We found a poor correlation between patients'  $\text{FEV}_1$  and FVC values and exercise capacity. This is consistent with recent studies showing that hypoxemia, and not respiratory mechanics, predominantly limit maximal incremental exercise in patients with IPF (23,24).

We found a good correlation in IPF patients between baseline levels of hypoxia and performance distance on the SWT, suggesting that supplemental oxygen may result in improvements in exercise tolerance and dyspnoea in this patient population. This hypothesis is supported by recent studies showing that supplemental oxygen improves maximal exercise performance in patients with interstitial lung disease (23,24), and also that the greatest benefit with supplemental oxygen was in subjects with more severe disease, as evidenced by a reduced  $\text{DL}_{\text{CO}}$  (23,24).

This data also demonstrates a significant correlation between  $DL_{CO}$  and performance distance on the SWT. This is important for two reasons. Firstly, in a study evaluating lung function in IPF and referral for lung transplantation, Mogulkoc *et al.* (25) showed using receiver operating characteristic (ROC) curve analysis that  $DL_{CO}$  was the most important predictor of survival in IPF. Secondly, King *et al.* (26) recently demonstrated using a more complex clinical, radiological and physiological (CRP) score, that  $VO_2$  max was a major variable in determining a CRP score utilized to predict survival in IPF. Therefore the significant relationship between exercise and  $DL_{CO}$  in this study suggests that SWT may complement simple methods for predicting survival.

Simple exercise tests can be employed to reveal the true extent of disability and assess patients' ability to perform day-to-day activities. However, other exercise tests of disability, such as the 6 and 12 min walk tests have no standardized pace or incremental facility (3), and the lack of uniform instructions for operators or patients results in a variety of test procedures being adopted. The SWT has the advantage in that it is standardized, incremental, and externally paced, diminishing the effect of the operator's influence. Unlike the 6 or 12 min walking tests where effort may be maximal from the start, the SWT stresses the patient progressively to a symptom-limited maximum. This gradual increase in exercise intensity increases the safety of the test. Moreover, an advantage of the shuttle walking test is that it has a better correlation with peak oxygen uptake than the 6 min walking test (27).

Maximal oxygen consumption has previously been measured during a corridor SWT in COPD patients using a portable oxygen consumption meter supported by a back pack, with the mouthpiece supported by a head harness (4). However, with this method there was a significant underestimation in ventilation by the portable meter, and patients consistently reported that the oxygen consumption equipment had inhibited their performance (4). Therefore, the most precise method of measuring  $VO_2$  max is by analysis of expired air during a maximal exercise laboratory test.

In summary, the present study substantiates the proposal that the SWT is a simple incremental maximal exercise test of disability that provides an objective measure of IPF patients' cardiorespiratory capacity. This provides a tool which may complement existing physiologic and radiological measures of disease progression as novel therapeutic agents for IPF are being developed.

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